

VISIT...

LANZAROTE
Caliente.COM

between the values of (2) and (10) support the suggestion⁵ that (d) may be implicated in the rearrangement. The enhanced loss of deuterium from the even-electron species is similar to that observed for the losses of Me[•] from the 9,10-dihydrophenanthrene^{10,11} and stilbene¹¹ molecular ions.

The hydrogen and carbon scrambling which precedes the losses of Me[•] from *m/e* 167 and *m/e* 168 can be explained by

TABLE 2

Abundances of $M - CH_2D_{2-3}$ for (2) and (10) at 15 ev						
Compound	$M - CH_2D_{2-3}$ Found			$-CH_2D_{2-3} - CHD_{2-3} - CD_3$ Calculated		
(2)	21	38	31.5	9.5	15	48
(10)	20	37	33	10	32	5

the reversible processes (a) → (b) and (c) → (d)^{5,12} with the central carbon unit (together with its substituents) inserting randomly into each C-C bond of the phenyl ring. This is likely to be accompanied by independent scrambling of the hydrogens of the seven and six carbon units during each cycle [e.g. (a) → (b)]. Our carbon scrambling observations are analogous to results obtained for (α,1-¹³C₂)toluene,¹³ and should be contrasted with loss of Ph[•] from the diphenylmethane 1-¹³C molecular ion, which occurs with no loss of the label (cf. ref. 6). We also suggest that ¹³C labelling data for the losses of Me[•] from the *o*-terphenyl¹⁴ and triphenylmethane¹² molecular ions are consistent with complete carbon scrambling.

(Received, March 4th, 1970; Com. 310.)

¹ Previous paper in this series, *Org. Mass Spectrometry*, in the press.

² S. Meyerson, H. Drews, and E. K. Fields, *J. Amer. Chem. Soc.*, 1964, 86, 4964.

³ J. H. D. Eland and C. J. Danby, *J. Chem. Soc.*, 1965, 5935.

⁴ R. A. W. Johnstone and B. J. Millard, *Z. Naturforsch.*, 1966, 21a, 604.

⁵ D. H. Williams, R. S. Ward, and R. G. Cooks, *J. Chem. Soc. (B)*, 1968, 522.

⁶ S. Meyerson, H. Hart, and L. C. Leitch, *J. Amer. Chem. Soc.*, 1968, 90, 3419.

⁷ J. Lesko, V. Vesely, and S. Korcek, *Coll. Czech. Chem. Comm.*, 1969, 34, 2836.

⁸ A. H. Struck and H. W. Major, jun., Paper presented to the ASTM E 14 Meeting, May 18–23, 1969, Dallas, Texas.

⁹ E. Tajima and J. Seibl, *J. Mass Spectrometry and Ion Physics*, 1969, 3, 245, references therein.

¹⁰ A. Maquestiau, Y. van Haverbeke, and F. Delalieu, *Bull. Soc. chim. belges*, 1968, 77, 355; 1969, 78, 589.

¹¹ P. F. Donaghue, P. Y. White, J. H. Bowie, B. D. Roney, and H. J. Rodda, *Org. Mass Spectrometry*, 1969, 2, 1061.

¹² K. D. Berlin and R. D. Shupe, *Org. Mass Spectrometry*, 1969, 2, 447.

¹³ K. L. Rinehart, A. C. Buchholz, G. E. van Lear, and L. C. Cantrell, *J. Amer. Chem. Soc.*, 1968, 90, 2983.

¹⁴ A. Copet and S. Facchetti, *Org. Mass Spectrometry*, 1968, 1, 881.

The Structure of Seararine, an Indole Alkaloid from *Rhazya stricta*

By YUSUF AHMAD and P. W. LE QUESNE*

(Department of Chemistry, University of Michigan, Ann Arbor, Michigan 48104)

and N. NEUSS

(Lilly Research Laboratories, Indianapolis, Indiana 46206)

Summary Seararine, a phenolic indole alkaloid from *Rhazya stricta*, is shown to be 10-hydroxyakuammicine (I).

SEARARINE, a new alkaloid from *Rhazya stricta*, has been shown¹ to be a C₂₀H₂₂N₂O₃ compound on the basis of analyses and mass spectra. We now present new data which show that seararine is a phenolic 2-methyleneindoline alkaloid of the akuammicine type, and has structure (I).

Seararine, m.p. 245° (decomp.), gave a monohydrochloride salt, m.p. 210° (decomp.), [α]_D²⁵ -724° (EtOH), λ_{max} (MeOH) 220, 311, 340 nm (ε 10,800, 14,400, 11,900) ν_{max} (Nujol) 3280 (N-H), 1675 (αβ-unsaturated ester -C=O), 1600, 1572 cm⁻¹ (exocyclic and aromatic -C=C-). Electrometric titration† indicated one basic pK_a' of 7.7 (66% Me₂N-CHO) with A.M.W. 370 (calc., 374). These data, together with the strikingly high negative specific rotation, suggest the presence of an akuammicine (II) skeleton.²⁻⁵ The mass spectrum further corroborates this assignment, since prominent peaks were observed at *m/e* 92, 107, and 121, as for akuammicine itself.⁶ The n.m.r. spectrum of seararine hydrochloride in CD₃OD

showed the presence of only three aromatic protons in a 1,2,4-pattern. Other signals revealed the presence of a methoxycarbonyl group (3H, s, τ 6.31) and an ethylidene group (1H, q, τ 4.20, J 6Hz, and 3H, d, τ 8.60, J 6Hz). These data correspond to those for these functional groups in other akuammicine alkaloids. The lack of a fourth aromatic proton is due to the presence of a phenolic hydroxyl group, which was demonstrated in several ways. First, the u.v. spectrum of seararine undergoes a bathochromic shift in alkaline solution [to λ_{max} 324, 363 nm (ε 12,200, 9500)]. Secondly, the methiodide¹ (III) of seararine revealed on electrometric titration only one acidic pK_a' of 12.1 (Ar-OH) (A.M.W. 512; calc. for C₂₁H₂₅IN₂O₃·CH₃OH, 512). With MeI-MeONa seararine gave the ON-dimethyl quaternary iodide (IV), C₂₂H₂₇N₂O₃I, m.p. 243–244° (decomp.), whose n.m.r. spectrum (CD₃OD) showed 3H singlets at τ 6.17 and 6.35 from the new O- and N-methyl groups, respectively. The N-methyl signal in the salt (III) was at τ 6.56. The methoxycarbonyl group of seararine, as in other akuammicine alkaloids, was lost on treatment with HCl (sealed tube), giving desmethoxycarbonylseararine (V), C₁₈H₂₀N₂O, m.p. 206° (decomp.).

The C-10 position for the phenolic hydroxyl in seararine

† Precipitation of the compound at pH 12 did not permit determination of the acidic pK_a', and required the use of the quaternary salt (III) for this determination.

was revealed by comparison of the chemical shifts of the aromatic protons of vindoline (VI), ibogaine, (VII), and sewaraine (I; $R^2 = H_a$) hydrochloride (see below). These

of spectra by members of the Molecular Structure Group, Lilly Research Laboratories, and the award of a Fulbright Hays Fellowship (to Y.A.).

Chemical shifts of aromatic protons (τ units)

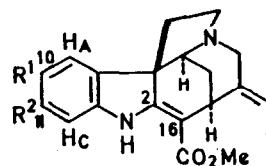
	H_A	J_{AB}	H_B	J_{BO}	H_C	Solvent
Vindoline	3.09	8Hz	3.70	2Hz	3.92	$CDCl_3$
Ibogaine	3.05	2Hz	3.25	9Hz	2.92	$CDCl_3$
Sewaraine hydrochloride ..	3.02	2Hz	3.30	7Hz	3.17	CD_3OD

data are also in accord with those of Witkop and his co-workers^{7,8} for other hydroxylated indole derivatives. Further corroboration is given by the magnitude of the bathochromic shift of the u.v. spectrum of sewaraine in alkaline solution, which is much closer to that of *p*-hydroxyaniline [λ_{max} (EtOH, neutral) 232, 300 nm (ϵ 7450, 2320) $\rightarrow$ λ_{max} (EtOH, alkaline) 248, 314 nm (ϵ 10,800, 2240)] than to that of *m*-hydroxyaniline [λ_{max} (EtOH, neutral) 234, 285 nm (ϵ 6130, 2160) $\rightarrow$ λ_{max} (EtOH, alkaline) 240, 293 nm (ϵ 7000, 3090)]. In addition, the mass spectrum of sewaraine (I) showed no significant peaks due to the loss of OH or H_2O , whereas that of the aliphatic hydroxyakuammicine mossambine (VIII)⁹ showed an $M - 17$ peak at m/e 321, ascribable to the loss of OH. High resolution mass spectrometry of sewaraine disclosed a small peak at m/e 146.06487 (calc. for $C_{20}H_{24}ON$: 146.06059), which is assigned to the fragment (IX).

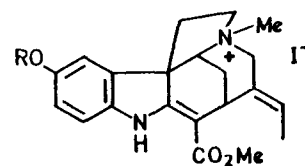
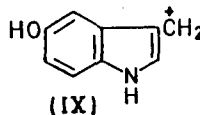
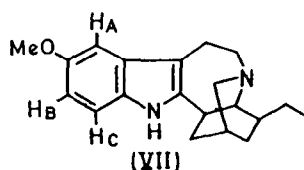
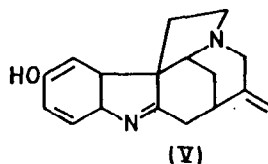
Treatment of sewaraine with $NaBH_4$ in aqueous acid solution gave the 2,16-dihydro-compound (X), $C_{20}H_{24}N_2O_3$, m.p. 202° (decomp.), [ν_{max} (Nujol) 1735 cm^{-1} (saturated ester $-C=O$)], whose mass spectrum was closely analogous to that of 2,16-dihydroakuammicine, (XI)⁸ except for the displacement by 16 mass units of characteristic fragments incorporating the indole nucleus at m/e 144 and 251 in (XI) to m/e 160 and 267 respectively in (X). Other fragments at m/e 130, 139, and 194, arising from the aliphatic portions of the molecules, were common to both spectra.

Our results thus indicate that sewaraine is 10-hydroxyakuammicine (I). The 11-hydroxyakuammicine structure (XII) has recently been assigned to vinervine, which occurs with its methyl ether vinervinine (XIII) in *Vinca erecta*.^{10,11}

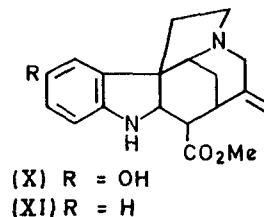
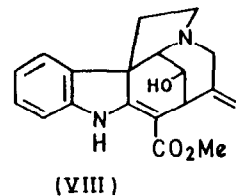
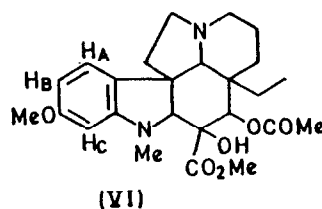
We gratefully acknowledge generous gifts of mossambine from Dr. A. Hofmann and Dr. X. Monseur, the recording



- (I) $R^1 = OH, R^2 = H$
 (II) $R^1 = R^2 = H$
 (XII) $R^1 = H, R^2 = OH$
 (XIII) $R^1 = H, R^2 = OMe$



- (III) $R = H$
 (IV) $R = Me$



- (X) $R = OH$
 (XI) $R = H$

(Received, March 9th, 1970; Com. 336.)

¹ S. Siddiqui, Y. Ahmad, and M. I. Baig, *Pakistan J. Sci. Indust. Res.*, 1966, 9, 97.

² K. Aghoramurthy and R. Robinson, *Tetrahedron*, 1957, 1, 172.

³ K. Bernauer, W. Arnold, C. Weissmann, H. Schmid, and P. Karrer, *Helv. Chim. Acta*, 1960, 43, 717.

⁴ P. N. Edwards and G. F. Smith, *J. Chem. Soc.*, 1961, 152.

⁵ J. Lévy, J. Le Men, and M.-M. Janot, *Bull. Soc. chim. France*, 1960, 979.

⁶ H. Budzikiewicz, J. M. Wilson, C. Djerassi, J. Lévy, J. Le Men, and M.-M. Janot, *Tetrahedron*, 1963, 19, 1265.

⁷ F. Märki, A. B. Robertson, and B. Witkop, *J. Amer. Chem. Soc.*, 1961, 83, 3341.

⁸ J. W. Daly and B. Witkop, *J. Amer. Chem. Soc.*, 1967, 89, 1032.

⁹ X. Monseur, R. Goutarel, J. Le Men, J. M. Wilson, H. Budzikiewicz, and C. Djerassi, *Bull. Soc. chim. France*, 1962, 1088.

¹⁰ P. Kh. Yuldashev, U. Ubaev, M. A. Kuchenkova, and S. Yu. Yunusov, *Khim. prirod. Soedinenii*, 1965, 1, 34.

¹¹ N. Abdurakhimova, P. Kh. Yuldashev, and S. Yu. Yunusov, *Dokl. Akad. Nauk S.S.S.R.*, 1967, 173 (1), 87.